

APPLICANT(S): Steiner et al.,
SERIAL NO.: 09/449,817
FILED: November 29, 1999
Page 2

In the Specification:

Please amend page 22, line 20 as follows:

See, e.g., ~~Sambrook et al., 1989~~ or Ausubel et al., 1992

Please amend page 25, lines 24-25 as follows:

See *PCR Protocols: A Guide to Methods and Applications* ~~[74]~~.

Please amend page 25, line 31 to page 26 line 6 as follows:

Oligonucleotides for use as probes or PCR primers are chemically synthesized according to the solid phase phosphoramidite triester method, or first described by Beaucage and Carruthers [19] using an automated synthesizer, ~~as described in Needham-VanDevanter [69]~~. Purification of oligonucleotides is by either native acrylamide gel electrophoresis or by anion-exchange HPLC ~~as described in Pearson, J.D. and Regnier, F.E. [75A]~~. The sequence of the synthetic oligonucleotide can be verified using ~~[[the]]~~ a chemical degradation method of Maxam, A.M. and Gilbert, W. [63].

Please amend page 26, lines 8-9 as follows:

High stringent hybridization conditions are selected at about 5~~[[?]]~~°C lower than the thermal melting point (T_m) for the specific sequence at a defined ionic strength and pH.

Please amend page 26, lines 11-13 as follows:

Typically, stringent conditions will be those in which the salt concentration is at least about 0.02 molar at pH 7 and the temperature is at least about 60~~[[?]]~~°C.

Please amend page 26, lines 17-19as follows:

APPLICANT(S): Steiner et al.,
SERIAL NO.: 09/449,817
FILED: November 29, 1999
Page 3

For Example high stringency may be attained for example by overnight hybridization at about 68°C in a 6x SSC solution, washing at room temperature with 6x SSC solution, followed by washing at about 68°C in a 6x SSC in a 0.6x SSX solution.

Please amend page 26, lines 25-26 as follows:

5) wash 4x for 1 minute each at room temperature at 4x at 60[[]]°C for 30 minutes each;

Please amend page 27, lines 7-8 as follows:

For discussions of nucleic acid probe design and annealing conditions, see, for example, ~~Sambrook et al., [81]~~ or Ausubel, F., et al., [8].

Please amend page 28, lines 11-14 as follows:

DNA fragments can be prepared, for example, by digesting plasmid DNA, or by use of PCR, or synthesized by either [[the]] a phosphoramidite method ~~described by Beaucage and Carruthers, [19]~~, or by [[the]] a triester method ~~according to Matteucci, et al., [62]~~, both ~~incorporated herein by reference.~~

Please amend page 32, lines 9-11 as follows:

~~See Harlow and Lane [32] for a description of immunoassay formats and conditions that can be used to determine specific immunoreactivity.~~

Please amend page 33, lines 31-34 as follows:

A description of a radioimmunoassay (RIA) may be found in *Laboratory Techniques in Biochemistry and Molecular Biology* [[[52]]], with particular reference to the chapter entitled "An Introduction to Radioimmune Assay and Related Techniques" by Chard, T., incorporated by reference herein.

Please amend page 34, lines 8-9 as follows:

APPLICANT(S): Steiner et al.,
SERIAL NO.: 09/449,817
FILED: November 29, 1999
Page 4

~~A general overview of the applicable technology is in Harlow and Lane [32], incorporated by reference herein.~~

Please amend page 34, line 18 as follows:

~~For competitive immunoassays, see Harlow and Lane [32] at pages 567-573 and 584-589.~~

Please amend page 34, lines 30-32 as follows:

Briefly, spleen cells or other lymphocytes from an animal immunized with a desired antigen are immortalized, commonly by fusion with a myeloma cell ~~(see, Kohler and Milstein [50], incorporated herein by reference).~~

Please amend page 35, lines 8-9 as follows:

~~See for example: McCafferty, J *et al.* [64]; Hoogenboom, H.R. *et al.* [39]; and Marks, J.D. *et al.* [60].~~

Please amend page 35, lines 28-29 as follows:

~~See [81] *supra*, for details concerning selection markers and promoters for use in *E. coli*.~~

Please amend page 36, lines 10-11 as follows:

~~See, for instance, Scopes, R. [84], incorporated herein by reference.~~

Please amend page 61, lines 16-21 as follows:

The probes of the invention may be synthesized enzymatically, using methods well known in the art (*e.g.*, nick translation, primer extension, reverse transcription, the polymerase chain reaction, and others) or chemically (*e.g.*, by methods such as [[the]] phosphoramidite method described by Beaucage and Carruthers [19], or by [[the]] a triester method according to Matteucci, *et al.* [62], both incorporated herein by reference).

APPLICANT(S): Steiner et al.,
SERIAL NO.: 09/449,817
FILED: November 29, 1999
Page 5

Please amend page 61, lines 6-12 as follows:

~~In situ~~ PCR is described in Neuvo *et al.* [71], Intracellular localization of polymerase chain reaction (PCR) amplified Hepatitis C cDNA; Bagasra *et al.* [10], Detection of Human Immunodeficiency virus type 1 provirus in mononuclear cells by ~~in situ~~ polymerase chain reaction; and Heniford *et al.* [35], Variation in cellular EGF receptor mRNA expression demonstrated by ~~in situ~~ reverse transcriptase polymerase chain reaction. ~~In situ~~ hybridization assays are well known and are generally described in the literature ~~Methods Enzymol.~~ [67] incorporated by reference herein.

Please amend page 63, line 13 as follows:

~~See Wickstrom E.L., *et al.* [93] and Harel-Bellan, A., *et al.* [31A].~~